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Declaration under Rule 4.17:
— *of inventorship (Rule 4.17(iv)) for US only*

Published:
— *with international search report*

(88) Date of publication of the international search report:
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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

WO 2004/048393 A3

(54) Title: NOVEL INHIBITORS OF β-LACTAMASE

(57) Abstract: The invention relates to bacterial antibiotic resistance and, in particular, to compositions and methods for overcoming bacterial antibiotic resistance. The invention provides novel β-lactamase inhibitors, which are structurally unrelated to the natural product and semi-synthetic β-lactamase inhibitors presently available, and which do not require β-lactam pharmacophore. The invention also provides pharmaceutical compositions and methods for inhibiting bacterial growth.

INTERNATIONAL SEARCH REPORT

International Application No
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A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61K31/381 A61K31/4436 A61K31/4709 A61K31/662 C07D333/18
C07D333/20 C07D333/58 C07D213/34 C07D213/38 C07F9/38
C07F9/40 C07F9/58 C07F9/60 C07F9/6536 C07F9/6553

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61K C07D C07F

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
CHEM ABS Data, BIOSIS, EPO-Internal, MEDLINE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 6 472 406 B1 (BESTERMAN, JEFFREY M. ET AL) 29 October 2002 (2002-10-29) the whole document	7-32
X	WO 2001/002411 A (METHYLGENE INC., CAN.) 11 January 2001 (2001-01-11) the whole document	7-32
X	XIE, GUI-YANG ET AL: "Synthesis of a novel antigen containing phosphorus" CHEMICAL JOURNAL OF CHINESE UNIVERSITIES (GAODENG XUEXIAO HUAXUE XUEBAO) (2003), 24(6), 1037-1039, XP009029967 compound 4	1,3,4

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[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
14 May 2004	02/06/2004

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Elliott, A

Form PCT/ISA/210 (second sheet) (January 2004)

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	MAVEYRAUD, LAURENT ET AL: "Crystal Structure of an Acylation Transition-State Analog of the TEM-1.beta.-Lactamase. Mechanistic Implications for Class A.beta.-Lactamases" BIOCHEMISTRY (1998), 37(8), 2622-2628 , XP002280293 Scheme II	1-5,31, 32
A	LI, NAIXIN ET AL: "Structure-activity studies of the inhibition of serine.beta.-lactamases by phosphonate monoesters" BIOORGANIC & MEDICINAL CHEMISTRY (1997), 5(9), 1783-1788, XP002100230 Compound 14	1-5,31, 32
A	CHEN, CELIA C. H. ET AL: "Structure of a phosphonate-inhibited.beta.-lactamase. An analog of the tetrahedral transition state/intermediate of.beta.-lactam hydrolysis" JOURNAL OF MOLECULAR BIOLOGY (1993), 234(1), 165-78, XP002280294 figure 2	1-5,31, 32
A	RAHIL, JUBRAIL ET AL: "Characterization of covalently bound enzyme inhibitors as transition-stat analogs by protein stability measurements: Phosphonate monoester inhibitors of.beta.-lactamase" BIOCHEMISTRY (1994), 33(1), 116-25 , XP002963391 Compounds 15 & 17	1-5,31, 32
A	RAHIL, JUBRAIL ET AL: "Structure-activity relationships in the inhibition of serine.beta.-lactamases by phosphonic acid derivatives" BIOCHEMICAL JOURNAL (1993), 296(2), 389-93, XP009029976 Compounds 11 & 13	1-5,31, 32
A	RAHIL, JUBRAIL ET AL: "Mechanism of inhibition of the class C.beta.-lactamase of Enterobacter cloacae P99 by phosphonate monoesters" BIOCHEMISTRY (1992), 31(25), 5869-78, XP002280295 Compound 5	1-5,31, 32

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	RAHIL, J. ET AL: "Intramolecular participation of the amide group in acid- and base-catalyzed phosphonate monoester hydrolysis" JOURNAL OF THE CHEMICAL SOCIETY, PERKIN TRANSACTIONS 2: PHYSICAL ORGANIC CHEMISTRY (1972-1999) (1991), (7), 947-50, XP009029952 Compound 2g	1-5,31, 32

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 03/36929

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.: –
because they relate to subject matter not required to be searched by this Authority, namely:

see FURTHER INFORMATION sheet PCT/ISA/210

2. [ ] Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.1

Although claim 32 is directed to subject-matter comprising a method of treatment of the human and/or animal body, the search has been carried out and based on the alleged effects of the compounds of the application.

Continuation of Box I.1

Rule 39.1(iv) PCT - Method for treatment of the human or animal body by therapy (claim 32)

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 03/36929

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
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